Replication Stress and Telomere Dysfunction Are Present in Cultured Human Embryonic Stem Cells.

Journal: Cytogenet Genome Res

Publication Year: 2015

Authors: Christine Janson, Kristine Nyhan, John P Murnane

PubMed link: 26517359

Funding Grants: Genomic instability during culturing of human embryonic stem cells

Public Summary:
Replication stress causes DNA damage at fragile sites in the genome. DNA damage at telomeres can initiate breakage-fusion-bridge cycles and chromosome instability, which can result in replicative senescence or tumor formation. Little is known about the extent of replication stress or telomere dysfunction in human embryonic stem cells (hESCs). hESCs are grown in culture with the expectation of being used therapeutically in humans, making it important to minimize the levels of replication stress and telomere dysfunction. Here, the hESC line UCSF4 was cultured in a defined medium with growth factor Activin A, exogenous nucleosides, or DNA polymerase inhibitor aphidicolin. We used quantitative fluorescence in situ hybridization to analyze individual telomeres for dysfunction and observed that it can be increased by aphidicolin or Activin A. In contrast, adding exogenous nucleosides relieved dysfunction, suggesting that telomere dysfunction results from replication stress. Whether these findings can be applied to other hESC lines remains to be determined. However, because the loss of telomeres can lead to chromosome instability and cancer, we conclude that hESCs grown in culture for future therapeutic purposes should be routinely checked for replication stress and telomere dysfunction.

Scientific Abstract:
Replication stress causes DNA damage at fragile sites in the genome. DNA damage at telomeres can initiate breakage-fusion-bridge cycles and chromosome instability, which can result in replicative senescence or tumor formation. Little is known about the extent of replication stress or telomere dysfunction in human embryonic stem cells (hESCs). hESCs are grown in culture with the expectation of being used therapeutically in humans, making it important to minimize the levels of replication stress and telomere dysfunction. Here, the hESC line UCSF4 was cultured in a defined medium with growth factor Activin A, exogenous nucleosides, or DNA polymerase inhibitor aphidicolin. We used quantitative fluorescence in situ hybridization to analyze individual telomeres for dysfunction and observed that it can be increased by aphidicolin or Activin A. In contrast, adding exogenous nucleosides relieved dysfunction, suggesting that telomere dysfunction results from replication stress. Whether these findings can be applied to other hESC lines remains to be determined. However, because the loss of telomeres can lead to chromosome instability and cancer, we conclude that hESCs grown in culture for future therapeutic purposes should be routinely checked for replication stress and telomere dysfunction.